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Evidence for Spread of the Human Immunodeficiency Virus Epidemic into Low Prevalence Areas of the United States

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Summary: Reports of an increased proportion of AIDS cases occurring in small and medium-sized cities suggest that the HIV epidemic may be spreading into locations that were previously characterized by their low HIV antibody prevalences. Studying the question of the geographic spread of the HIV infection epidemic (rather than the AIDS epidemic) has been difficult largely because most serial seroprevalence data have been gathered from cohorts of high risk individuals (e.g., homosexual/bisexual cohorts) in New York City, San Francisco, and other geographically circumscribed areas. The U.S. military applicant HIV screening data were used in the current report to examine rates and 24 month temporal trends in geographic areas characterized by their HIV endemicities. The data examined concern the seven most populous states and four hyperendemic metropolitan areas located within those states (New York City, Miami, Houston, and San Francisco). In the nonepidemic regions, seroprevalence rates increased among black and white applicants. In the four epidemic urban areas, only young black applicants had higher HIV seroprevalence rates during the second 12 month period. Six of the seven nonepidemic regions had positive HIV seroprevalence trends, and these trends were significant in Florida, California, Texas, Illinois, and Ohio. The increases in these regions were greater for young blacks (30% excess for year 2 vs. year 1) compared to young whites (12% excess for year 2 vs. year 1). These data provide evidence of birth year specific increases in seroprevalence over time occurring in presumed low HIV prevalence areas. These increases cannot be due to, but are observed in spite of, biases associated with increasing self-selection over time. Key Words: Epidemiology—HIV seroprevalence—Geographic trends—Military applicants.

Estimates of trends in HIV seroprevalence for large samples of the U.S. population are vital to the national effort to conduct surveillance of this disease. While extrapolations from AIDS case data are useful for very short periods of time, they are based on infections acquired many years in the past and give no indication of the present trends in HIV infection, trends that are vital for assessing the current infection epidemic.

Since the epidemic began in a few large cities such as New York, San Francisco, and Miami, it is important to determine whether the infection epi-

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demic is still concentrated in a few hyperendemic cities, or whether many of the new infections are occurring in locations remote from the original epidemic foci. This has been a particularly difficult question to address with existing HIV infection data. For instance, the estimates of declining incidence of new HIV cases from small homosexual/bisexual cohorts within individual cities, for example, in San Francisco and New York City (1–3), must be reconciled with projections of increasing numbers of HIV cases among intravenous drug abusers (4,5). A report of increasing proportions of CDC-reported AIDS cases from small and medium-sized cities (6) suggests that HIV antibody trends based on traditional endemic locations may not generalize to the rest of the country. Without serial HIV seroprevalence data from geographically dispersed locations, it has not been possible to estimate the degree to which the infection epidemic may be involved in a similar shift to less populous locations. The CDC "family of seroprevalence surveys" at dispersed sites in the U.S. will provide useful data regarding geographic distribution and spread over the coming years.

In this report, we examine temporal trends in the HIV infection epidemic and whether these trends support the hypothesis that the HIV infection epidemic is spreading to less populous locations based on data collected during the period 1985–1987. Using data from the first 2 years of military applicant screening, we have examined the seven most populous states in the U.S. in order to have sufficient power to determine trends. Given estimates of a national prevalence of HIV in the range of 1.4 to 3.0 per 1,000 persons (7–9), attempts to estimate rates and trends for large geographic areas must concern data on several hundred thousand persons. This report examines data on 435,000 applicants from the seven most populous states, New York, California, Texas, Pennsylvania, Illinois, Ohio, and Florida.

METHODS

Applicant Population

All persons applying for military service are required to take a series of examinations to determine their fitness for service. Included among these exams are medical tests for the presence of a variety of conditions, including HIV infection. The evaluations are conducted at 71 military entrance processing stations (MEPS) located throughout the U.S. and its territories. The data routinely collected by the MEPS stations include age, ethnicity, home of record (by state, county, and zip code), and educational attainment. This is a very young population, with 82% of the applicants aged 25 years or less. Of the 1,278,319 applicants as of September 30, 1987, 86% were male and 73% were white. A previous report has described in detail the first 6 month's prevalence rates by age, ethnicity, sex, and location (9).

One of the major strengths of the HIV screening data from applicants for military service has been the uniform sampling approach across all geographic areas of the country. While the means by which manpower enters the military is not constant over long time periods, for the recent past the process of acquiring volunteers has remained constant and has been handled in the same way across all regions of the U.S.

We have divided the first 24 months of accumulated prevalence data into two 12 month periods: October 1, 1985, through September 30, 1986, and October 1, 1986, through September 30, 1987.

Formation of Subgroups

The overall prevalence rate may not be the most appropriate measure for a temporal trend analysis when the sampled population is exposed to selection biases that vary by birth cohort and over time. When that is the case, an analysis divided into birth year cohorts may be necessary.

We have split the applicant population into a younger cohort (birth years 1962–1969) and an older cohort (birth years prior to 1962) roughly equivalent to a cut point at age 25 years. There are two reasons for doing this. First, recruiters actively solicit 17–24-year-old individuals. Older individuals may apply, but are not targeted for recruitment, thus, older applicants may be less representative of the U.S. population of the same age than younger applicants. Secondly, HIV-related mortality is increasing rapidly in 15–64-year-old males (10), of whom 30–44-year-old individuals are the most affected. AIDS and other HIV-associated mortality is now the leading cause of death in males aged 25–44 years in New York City (11). Since death rates from other causes have been decreasing for this age group for many years (12), the increases in deaths in the future will be even more disproportionately due to HIV disease.

The age distributions of the applicant population and of the CDC-reported AIDS cases are shown in Fig. 1. The shaded portion of the military applicant age curve depicts the applicants 25 years of age and above at the time of enlistment. This shaded area falls in the middle of the CDC-reported AIDS age distribution. Thus, these individuals have the highest probability of experiencing clinically significant morbidity and mortality related to HIV. Since these probabilities increase over time, the probability of infected applicants excluding themselves because of HIV-associated morbidity may also increase. Minimization of the selection effects of increasing morbidity and mortality was achieved by dividing the analysis into separate birth year cohorts: a younger cohort with a median age of 19 years and an older cohort with a median age of 29 years.

To assess race-specific differences, prevalence data were summarized separately for blacks and whites. Other racial–ethnic groups, such as Hispanics, did not have sufficient numbers to allow for informative estimates after geographic subgrouping; for that reason, Hispanics are not presented as a separate subgroup.

Geographic subgroups were formed to isolate the four metropolitan areas with an elevated (at least double the 1985–1986 national average of 1.52 per 1,000) rate in 1985–1986 from the surrounding low

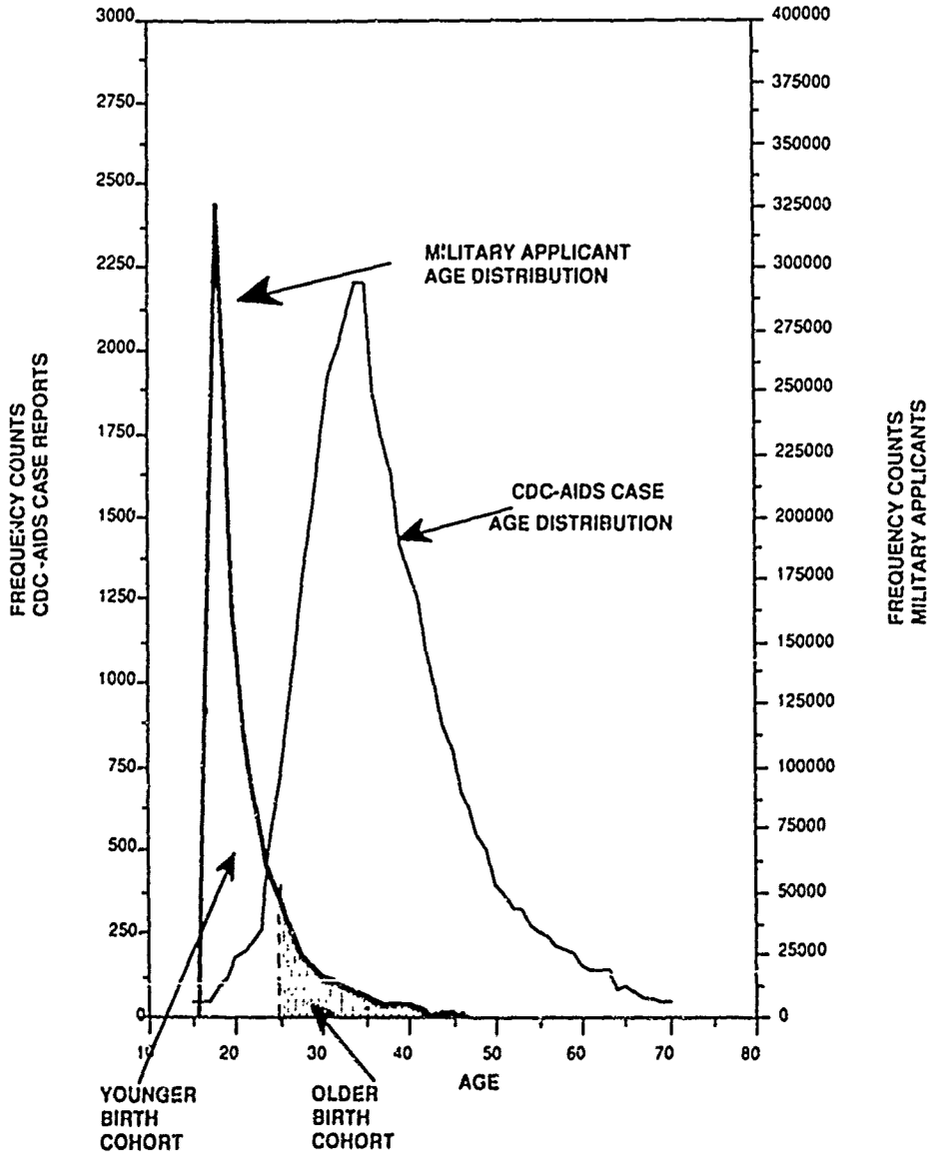

FIG. 1. Comparison of age distributions in CDC-reported AIDS cases vs. military applicants.

prevalence territory. For uniformity, we assigned all counties with a population centroid (the geographic center of population) within 75 miles of the center of an endemic area to the metropolitan endemic area (13). The rest of the state comprised those counties not included in the 75 mile metropolitan perimeter.

Effect of Selection Bias

There are several causes of changes in prevalence of antibody between time periods in birth year cohorts, but only two reflect true changes: (a) the occurrence of new infections (these always increase prevalence) and (b) deaths related to HIV (these always decrease prevalence).

There are several causes of apparent but not real changes in prevalence between time periods: (a) imprecise estimates of prevalence, (b) changes in the performance of the screening test, and (c) increasing or decreasing selection-out bias.

Of the three causes of apparent change in prevalence over time, we think that selection-out bias is likely to have increased over time and thus to have significantly affected the observed prevalence trends. However, it is important to realize that the effect of increasing selection out of infected individuals is to bias these trends towards the null (no trend). Positive trends in seroprevalence among military applicants almost certainly underestimate actual trends in their underlying populations.

Statistical Analyses

Prevalence rates for sub-state geographic areas were calculated as a geographical weighted average of the observed counties' prevalences and the prevalences from all geographically adjacent counties. This averaging damps the highs and lows for each time period, thus providing locally smoothed prevalence estimates. Comparisons of smoothed prevalence rates between two time periods were by a Pearson's χ^2 (14). Ninety-five percent confidence limits around rate ratios were calculated as ± 1.96 times the estimate of the standard error of the rate ratio, using the Taylor series approach to approximation of the variance at a rate ratio given by Kleinbaum, Kupper, and Morgenstern (15).

RESULTS

The 24 month average antibody prevalence for race and birth year cohorts of the applicant population are represented in Table 1. In addition to the relative size of the population of older applicants (17.5% of the total) compared to that of younger applicants (82.5% of the total), this table depicts the 10 year difference in median age between the younger and older cohorts.

Prevalence Trends in Seven States

The prevalence trends for combinations of specific race and birth year cohort subgroups are given in Figs. 2–6. Figure 2 (Miami and the rest of Florida) indicates that the total rate fell for Miami, but rose for the rest of Florida. This pattern was reflected in a fall in the rate for older individuals in the Miami area, but in a steep rise for older applicants outside of Miami. White rates fell for both parts of Florida, black rates rose sharply for both areas. Figure 3 (San Francisco and the rest of California) reveals total prevalence rates to have declined modestly in the San Francisco area while exhibiting an increase in the rest of California.

Figure 4 (New York City and the rest of New York State) shows a decline in total prevalence. The mixture of prevalence trends for New York City is such that the overall trend does not adequately mirror the race–birth year cohort trends. Increases were seen in the white ($p = 0.06$) and black ($p = 0.04$) prevalence rates. Countering this trend was a drop in the older applicant antibody prevalence from 15.9 to 14.8 per 1,000. The flat total prevalence trend in New York City is thus dominated by the trend in the older applicant cohort. For

TABLE 1. *24 month HIV antibody prevalence by birth year cohorts*

Cohort	Cases/tested	Rate/1,000	Median age (years)	Mean age (years)	Range (years)
Whites, 1962–1969	190/284,514	0.67	19	19.6	17–25
Blacks, 1962–1969	256/74,610	3.43	19	19.8	17–25
Older, 1937–1961	379/76,022	4.98	29	30.3	25–48
Total	825/435,146	1.89	20	21.4	17–48

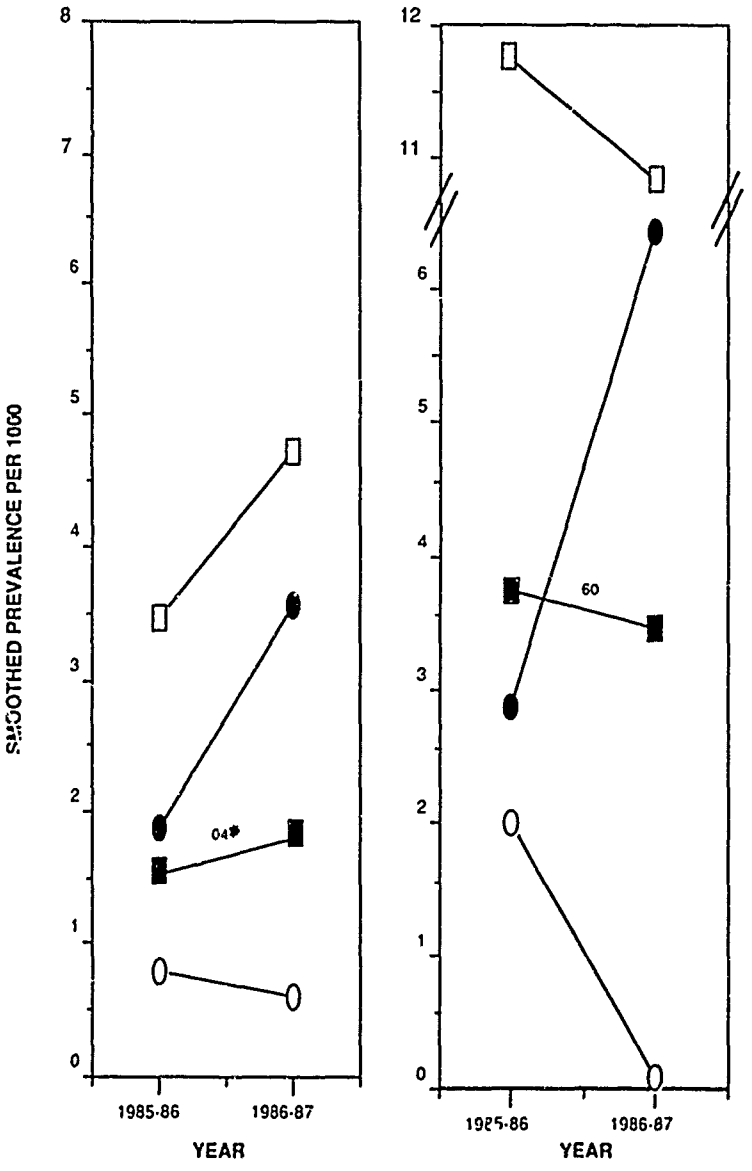

FIG. 2. Florida HIV antibody prevalence. Left: Florida excluding Dade County area; right: Dade County area. —●—, black; —○—, white; —□—, older; —■—, total. *p value from Pearson's χ^2.

the rest of New York State, a flat total trend was also apparent This trend was particularly influenced by the contribution of young white applicants, who made up 74% of all applicants in this region (compared to 41% in the New York City area).

Figure 5 (Houston and the rest of Texas) indicates that the overall trend was sharply lower for the Houston area, but it was up for the rest of Texas. Outside of the Houston area, divergent prevalence trends were seen. A very large increase (>300%) was evident for younger blacks, but a modest decrease (12%) occurred for whites during the same period.

Figure 6 presents trends for the state of Illinois. In this state, the modest downward trend in young blacks ($p = 0.17$) runs counter to a modest upward trend in young whites and to a sizeable upward trend in older individuals. Figure 6 also presents the trend data for Pennsylvania. As in many of the other locations, the downward trend in older individuals runs counter to an upward trend in young blacks and young whites. The total trend in Pennsylvania was flat, but this overall trend is heavily influenced by the downward trend in older individuals, who make up only 17% of the overall population, a strong upward trend was observed for young whites and blacks. The final panel depicts the

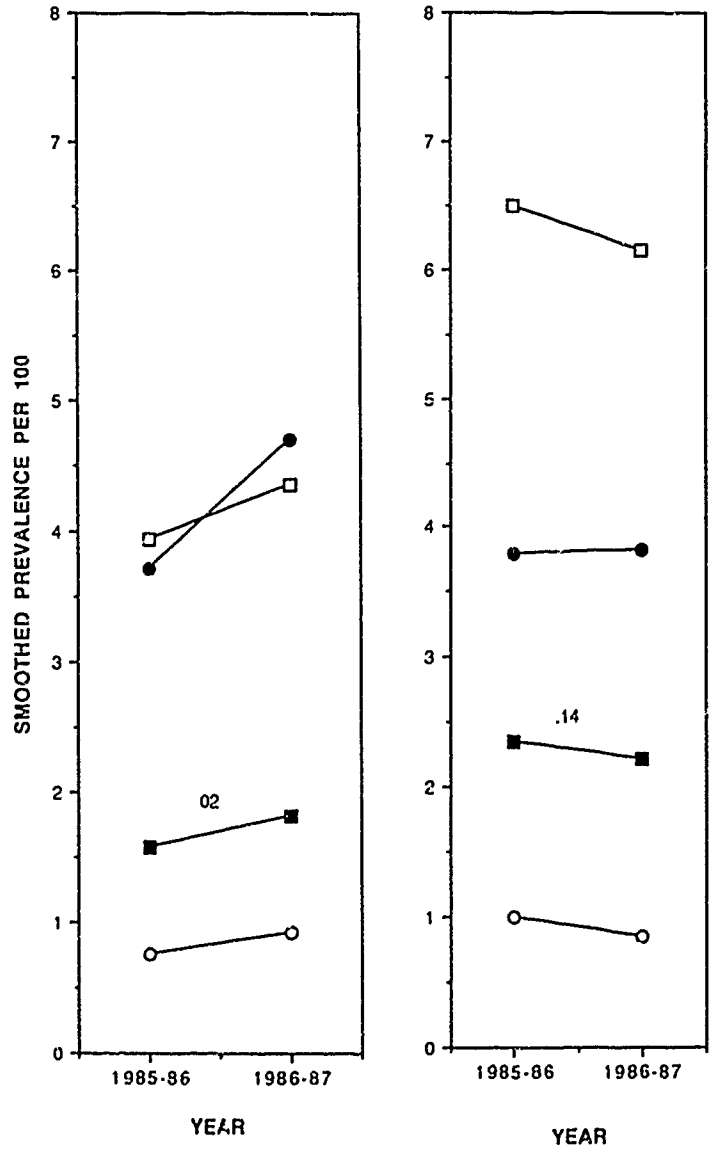

FIG. 3. California HIV antibody prevalence. See caption to Fig. 2 for definition of symbols. Left: California excluding San Francisco County area; right: San Francisco County area.

trends for the state of Ohio. The least populous of the seven states, Ohio had by far the lowest HIV antibody prevalence rates. However, the trends were consistently up across all race and birth year groups.

Prevalence Trends in Epidemic and Nonepidemic Areas

Table 2 summarizes prevalence trends for younger blacks, younger whites, and older applicants within all four epidemic urban areas pooled, as well as within the pooled nonepidemic areas. Contrary trends in the older birth year cohorts compared to the younger cohorts are apparent, particularly in urban epidemic areas. The overall prevalence in urban HIV epidemic areas is lower for the 1986–1987 time period. This is in marked contrast to the overall prevalence trend in nonepidemic areas.

The consistent pattern of increased seroprevalence observed in the aggregated nonepidemic areas (Table 2) was comprised of contributions by both black and white racial subgroups. Table 3 examines the race-specific prevalence ratios for the nonepidemic areas presented in Table 2. The overall year 2/year 1 prevalence ratio for blacks (1.30) was distributed fairly uniformly across the states, and the excess prevalence for year 2 was substantial and

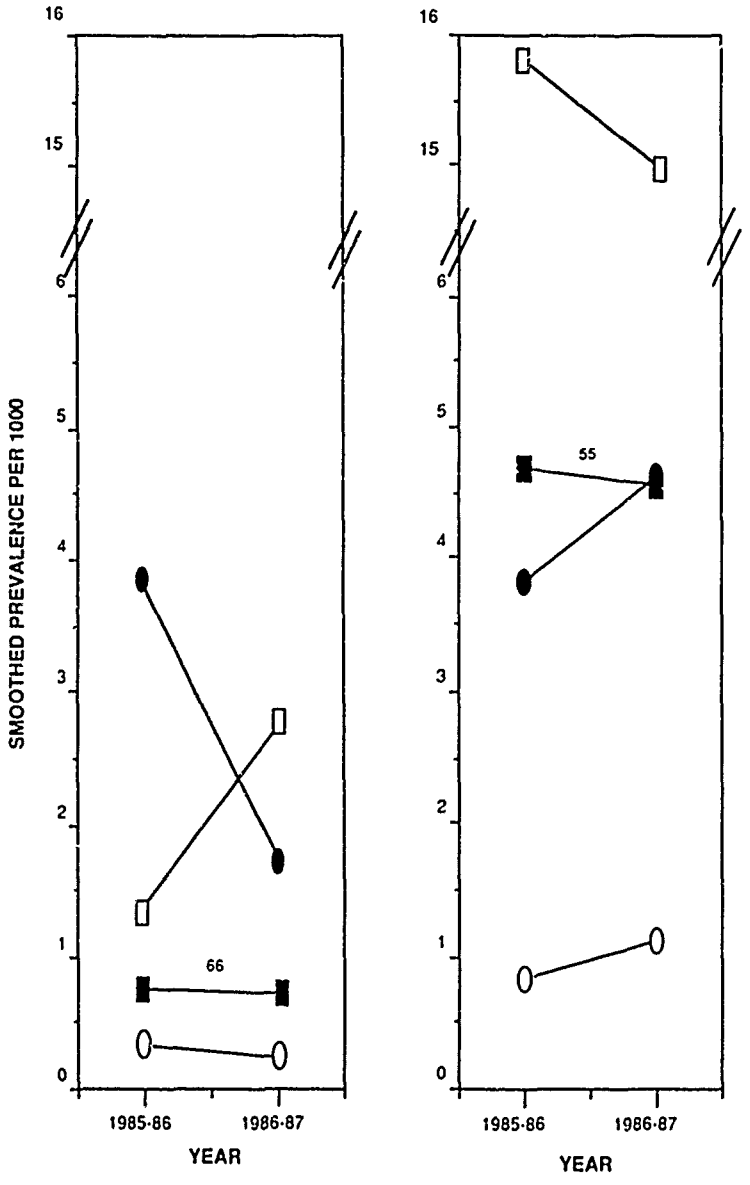

FIG. 4. New York HIV antibody prevalence. See caption to Fig. 2 for definition of symbols. Left: New York excluding New York City area; right: New York City area.

statistically significant in five of the six states with upward trends: Pennsylvania, Ohio, Texas, Florida, and California. The overall year 2/year 1 ratio for whites (1.12) was less significant in any individual state, but could be observed in California, Illinois, Pennsylvania, and Ohio.

DISCUSSION

A number of reports of time trends of HIV and antibody prevalence in prospectively followed groups in the United States have been published to date (1–3, 16–22). Of these studies, only the Winkelstein study attempted to use probability sampling to obtain volunteers (1,2). The McNeil study in the active-duty Army examined seroconversion in a population that was not selected on the basis of presumed risk (22). Other studies concerned cohorts of persons at increased risk: participants in hepatitis B vaccine trials (17,20), prospective evaluation of contacts of 45 AIDS cases (19), and prospective evaluation of 67 homosexual patients from a general medical clinic (16). Incidence among repeat blood donors, a group at decreased risk, has

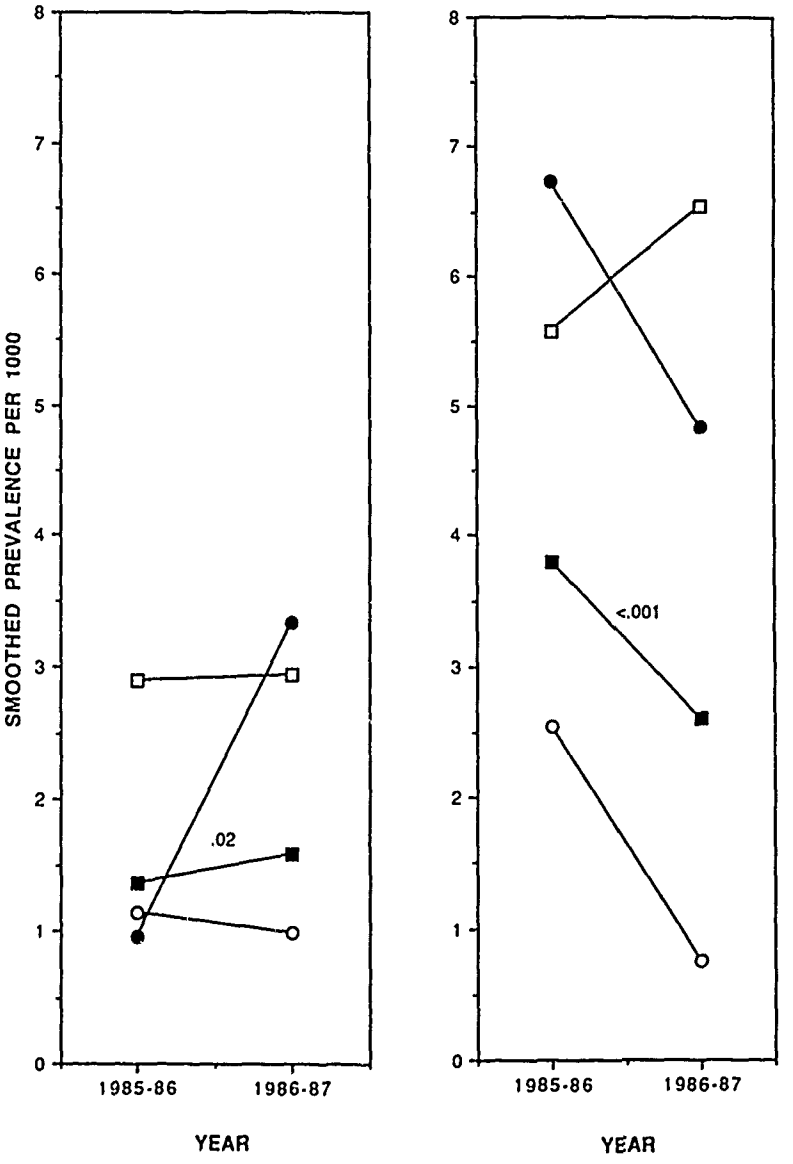

FIG. 5. Texas HIV antibody prevalence. See caption to Fig. 2 for definition of symbols. Left: Texas excluding Harris County area; right: Harris County area.

also been calculated (21). This relative scarcity of population-based studies reflects the difficulty and expense of assembling and following large population-based cohorts from which such data can be ascertained. Nevertheless, serial surveys over time, representing all geographic and demographic segments of the U.S., are vital if nationwide trends in the HIV infection epidemic are to be assessed.

The HIV infection epidemic is not now confined to the few urban centers where it was first reported (23–25). An extrapolation of geographic AIDS-reporting trends to the CDC predicted that by 1991 more than 80% of new AIDS cases would be reported from localities other than New York and San Francisco (4). However, monitoring the progress of the HIV epidemic from AIDS case data or from one-time or single-location cross-sectional surveys is difficult if not impossible. Serial serological surveys can provide reliable estimates of prevalence, cumulative incidence, and trends in HIV antibody positivity if a consistent sampling strategy is used. One such repeated nationwide serologic survey has been the screening program for civilian applicants for military service. A completely bias-free serologic survey of HIV infection in the U.S. does not exist; the military's applicant survey is no exception. Regulations that prohibit homosexual or bisexual men and intravenous drug abusers from serving in the military are likely to result in seroprevalence rates among military applicants that underestimate

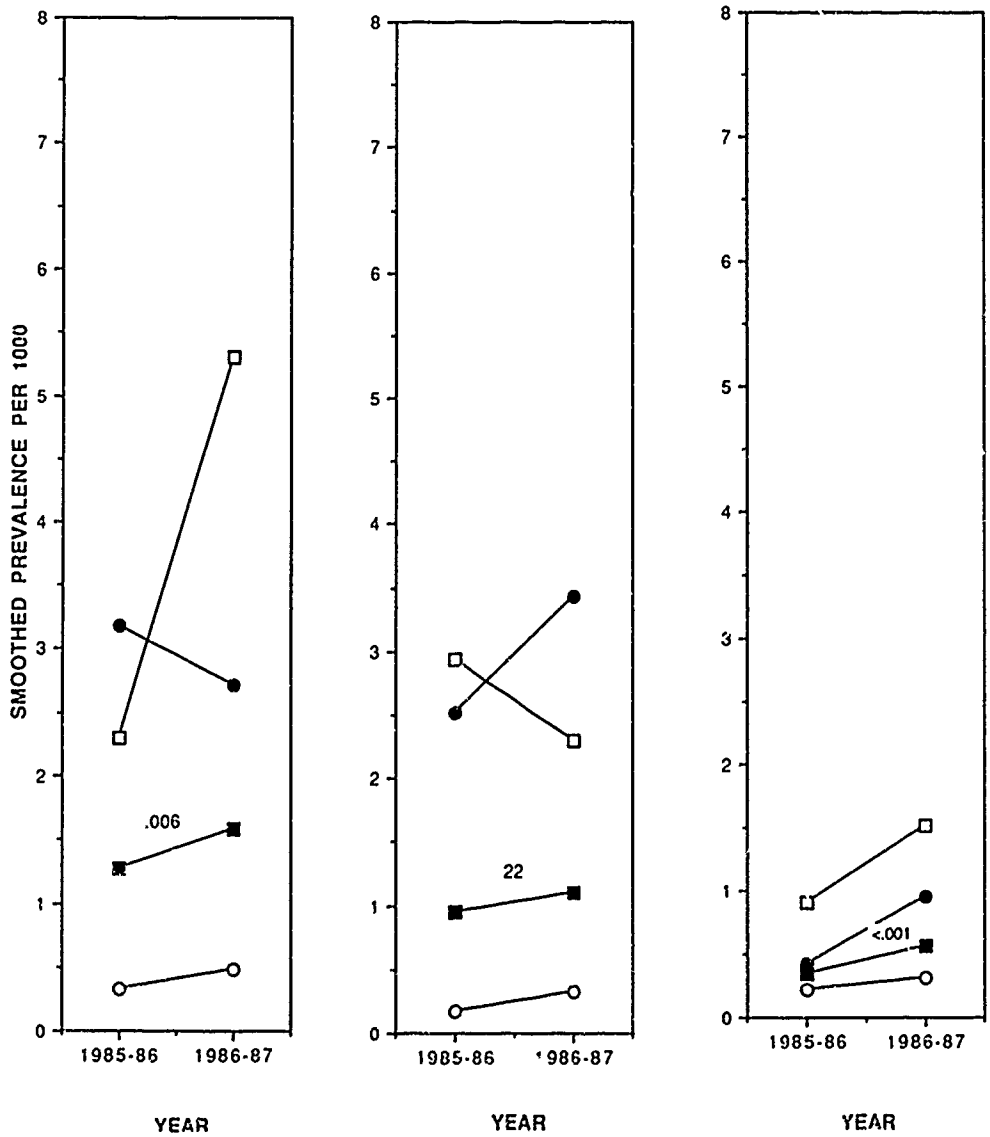

FIG. 6. HIV antibody prevalence. See caption to Fig. 2 for definition of symbols. Left. Illinois, center. Pennsylvania, right. Ohio.

those of the general populations. The underrepresentation of individuals with these traditional high risk behaviors for AIDS reflects an institutional selection bias that, if unchanged over time, would be of little use in estimating the direction of seroprevalence trends.

However, an important temporal trend occurring in all U.S. communities since 1985 has been an increasing knowledge of personal HIV status in young persons. Knowledge of HIV status is no longer uncommon. in one report from an emergency room in Baltimore, 22% of HIV-positive patients were aware of their condition (26). Knowledge increases have also been documented in a random sample of the U.S. population. For the period between May and October 1988, the National Health Interview Survey found that 26.8% of white respondents and 16.1% of black respondents aged 18–24 years had already been tested for the presence of HIV antibodies (Deborah Dawson, National Center for Health Statistics, personal communication). Furthermore, the proportions of whites tested were higher within five endemic metropolitan areas compared to the rest of the U.S. (30.2% vs. 26.4%). These nationwide data concerning increasing knowledge of HIV antibody status support our assumption of selection bias operating during the period 1985–1987, and that this bias would effectively

TABLE 2. *HIV antibody prevalance rates per 1,000 by birth year cohort, race, and location*

	Birth year cohorts						
	1962–69		Pre-1962				
	Blacks, cases/tested (rate)	Whites, cases/tested (rate)	Blacks, cases/tested (rate)	Whites, cases/tested (rate)	Total rate	Rate ratio[c]	95% confidence interval
Epidemic urban areas[a]							
1985–1986	46/9,950 (4.62)	37/19,808 (1.87)	69/2,741 (25.2)	37/5,085 (7.28)	189/37,584 5.03		
						0.88	(0.71, 1.09)
1986–1987	53/9,319 (5.69)	17/17,965 (0.95)	56/2,352 (23.8)	23/4,006 (5.74)	149/33,642 4.43		
Nonepidemic areas[b]							
1985–1986	69/27,935 (2.47)	68/130,580 (0.52)	45/6,576 (6.84)	51/27,934 (1.82)	233/193,025 1.21		
						1.23	(1.03, 1.47)
1986–1987	88/27,406 (3.21)	68/116,161 (0.59)	57/5,797 (9.83)	41/21,531 (1.90)	254/170,895 1.49		

[a] Miami, Houston, San Francisco, New York City.
[b] Low prevalence areas of Florida, New York, Texas, and California and entirety of Illinois, Ohio, and Pennsylvania.
[c] 1986–1987 vs. 1985–1986.

prescreen an increasing proportion of applicants, biasing trends in a general downward direction.

Given the likelihood of a general downward bias, with evidence of greater self-selection among whites and within endemic locations, certain conclusions can be made and others avoided. The increasing trend in low prevalence areas is apparent in spite of the conservative bias. The infection epidemic is now expanding outside of the original epidemic urban areas. This conclusion can be reached independent of the fact that we are less confident of the trend estimates from the endemic locations, given the greater influence of self-selection likely to be present in those locations.

The negative trends in white birth year cohorts can be attributed to selection bias, migrations, and HIV-associated deaths. The positive trends in the low prevalence areas and among black applicants in endemic cities are almost certainly affected by the same biases, but the NHIS data suggest that is so to a lesser degree. Self-selection biases aparently differ by race and geographic location; however, the direction of the bias is uniformly conservative. Given the differential knowledge of HIV status among blacks and whites over this time period, the apparently increasing relative risk between the races must be viewed with caution.

Published data on temporal trends in the HIV infection epidemic have thus far been derived from cohorts selected on the basis of presumed high or low risks, trends that are not directly referable to the U.S. population. Previous presentations of the military applicant data have concluded that no temporal trends were evident when analyzed by race and ethnicity or geographic region (27,28). An important limitation of these previously reported race-specific analyses, however, was that they were conducted on all birth years pooled, and over very large geographic areas. In view of the contrary trends in the younger and older birth year cohorts, and of the contrary within-state trends, it is unlikely that a simple age- and location-pooled analysis would detect any trends. The present analysis indicates a pronounced upward trend in seroprevalence for the young black cohort, regardless of geographic location. This consistent trend may reflect the increasing heterosexual transmission among adolescents and young adults of both sexes; another factor may

TABLE 3. *Race specific prevalence rate ratios for year 2 rate/year 1 rate in nonepidemic areas*

	CA	NY	TX	PA	IL	OH	FL	Total (95% C.I.)
Blacks	1.28[a]	0.46[b]	3.46[b]	1.36[a]	0.85	2.24[b]	1.89[b]	130 (0.95, 1.78)
Whites	1.23	0.68	0.88	1.92[a]	1.45	1.44	0.78	1.12 (0.80, 1.57)

[a] $p < 0.05$ (that the observed prevalence ratio was this different from 1.0 by chance).
[b] $p < 0.01$ (that the observed prevalence ratio was this different from 1.0 by chance).

be the continuing overrepresentation of young black males in the intravenous drug abuser population of the U.S. (23). Greater overlap of bisexual/homosexual males and intravenous drug abusers in some black communities has been suggested (29) and, if true, may mean greater mixing among infected individuals in black communities.

The emergence of regions outside the original AIDS epidemic centers as factors in the geography of AIDS has been described by Hyman and Stanley, who noted that non-metropolitan areas began to show growth of AIDS cases as a cubic function of time by 1984 (30). Other scientists have calculated the growth rates of CDC-reported AIDS cases, concluding that the growth rates are now higher in the nonurban reporting regions than in urban SMSAs in the West, South, or Central U.S. (31). The HIV seroprevalence data reported here, specifically the trends in applicants in Texas, Florida, and California, compared to those in New York, are consistent with these findings. These military applicant HIV antibody data document that HIV infection transmission was occurring in cities (and nonurban locations) outside the original AIDS epidemic centers as early as 2 years ago. Furthermore, the data indicate that transmission was occurring among adolescents and young adults both black and white, and across all regions of the U.S. If these findings can be replicated with more recent HIV seroprevalence data, it can be concluded that observations on the increasing proportion of AIDS cases in small cities are a significant development with serious health care ramifications for the future.

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